The Midnight-Noon Ebb-Flow Point Selection for 30 Cases of Acute Ischemic Cerebrovascular Diseases

Jiang Hua 姜华，Wang Manxia 王满侠，Guo Jian 郭健 & Li Zhidong 李志东
The Second Hospital of Lanzhou University, Lanzhou 730030, China

Objective: To observe the therapeutic effects of midnight-noon ebb-flow method of selecting acupoints (MNEFMSA) for acute ischemic cerebrovascular diseases (AICD) and its influence on hemorrheology and on the levels of interleukin-6 (IL-6), thromboxane B_2 (TXB_2) and 6-keto-prostaglandin $F_{1\alpha}$ (6-keto-$PGF_{1\alpha}$). **Methods**: The 90 cases were randomly divided into 3 groups, each consisting of 30 cases. The drug group was treated mainly by routine medication; in addition to medication, the affected-channel group was treated by acupuncture at points along the course of the affected channel, and the MNEFMSA group was treated by MNEFMSA. **Results**: The total effective rate of MNEFMSA group, affected-channel group and drug group was 96.67%, 90% and 73.33% respectively. The total effective rate of MNEFMSA group was obviously superior to that of the drug group ($P<0.01$), and cure rate and marked improvement rate were obviously superior to those of the drug group and the affected-channel group ($P<0.05$ or $P<0.01$). After treatment, the three groups all got improvements in the hemorheological indexes, of which MNEFMSA group got marked improvements in the whole blood viscosity and erythrocyte deformability rate, significantly different from the other two groups ($P<0.05$). At the early stage of treatment and after treatment, the three groups all had IL-6, TXB_2 and 6-keto-$PGF_{1\alpha}$ obviously improved ($P<0.05$ or $P<0.01$), of which MNEFMSA group got obvious improvement in 6-keto-$PGF_{1\alpha}$ and IL-6 ever since the early stage of the treatment ($P<0.05$). **Conclusions**: In the treatment of acute ischemic cerebrovascular diseases, MNEFMSA can markedly raise the clinical therapeutic effects by improving the hemorheological indexes, lowering the level of IL-6, and restoring the dynamic equilibrium between TXB_2 and 6-keto-$PGF1_{\alpha}$, so as to promote the recovery of cerebral nervous function.

Acute ischemic cerebrovascular diseases are frequently encountered in clinic. Data show that their onset tend to have diurnal rhythm difference, [1-3] which is related with the human 'biological clock'. Midnight-noon ebb-flow method of selecting acupoints (MNEFMSA) is adopted in the treatment here, and the comparison with control groups is conducted to observe the clinical effect and the influence on hemorrheology, interleukin-6 (IL-6), thromboxane B_2 (TXB_2) and 6-keto-prostaglandin $F_{1\alpha}$ (6-keto-$PGF_{1\alpha}$). The report is as follows.

CLINICAL MATERIAL

The 90 cases in this series were all inpatients in the Second Hospital of Lanzhou University in the period from May 1999 to August 2002. Of them, there were 56 males and 34 females, ranging in age from 41 to 82 years, with a mean of 57.8 years. All the patients got the acute onset and were hospitalized within 2 hours to 3 days after the attack. They were all diagnosed by CT and MRI as having acute ischemic cerebrovascular disease (cerebral thrombosis, cerebral infarction), with the diseases of heart, liver, kidney, lung, endocrine and metabolism excluded. The damage of nervous function was evaluated based on the *Evaluation Criteria for the Clinical Damage of Nervous Function of Cerebral Apoplexy Patient*

adopted at the Fourth National Academic Symposium on Cerebrovascular Diseases in 1995.[4] According to the TCM differentiation and based on the *Criteria for TCM Diagnosis and Therapeutic Effect*,[5] the patients were differentiated into 5 syndrome patterns: hyperactivity of liver-*yang* (14 cases), obstruction of collaterals by wind-phlegm (19 cases), phlegm-heat and excess of *fu*-organs (12 cases), *qi*-insufficiency and blood stasis (27 cases), and *yin*-deficiency with stirring of wind (18 cases). With the order of hospitalization, the drug group, affected-channel group and MNEFMSA group were formed randomly, each consisting of 30 cases. There were no significant statistical differences in sex, age, damage of nervous function and TCM syndromes among the three groups (P>0.05).

METHODS

All the patients were given the routine drug treatment with intravenous drip of dextran 40 added with compound salvia injection, and energy mixture added with citicoline. Patients accompanied with acute encephaledema were given mannitol by intravenous drip. The patients of drug group received only routine drug treatment. Based on routine drug treatment, the affected-channel group was given acupuncture, with the points selected from the affected channels, such as on the upper limb Jianyu (LI 15), Quchi (LI 11), Shousanli (LI 10), Waiguan (TE 5), Hegu (LI 4) and Houxi (SI 3), and on the lower limb Huantiao (GB 30), Futu (ST 32), Zusanli (ST 36), Yanglingquan (GB 34), Xuanzhong (GB 39), Sanyinjiao (SP 6) and Kunlun (BL 60). For patients with hyperactivity of liver-*yang*, Baihui (GV 20) and Taichong (LR 3) were added; for obstruction of collaterals by wind-phlegm, Fengchi (GB 20) and Fenglong (ST 40) were added; for phlegm-heat and excess of *fu*-organs, Dazhui (GV 14) and Tianshu (ST 25) were added; for *qi*-insufficiency and blood stasis, Zhongwan (CV 12) and Qihai (CV 6) were added; and for *yin*-deficiency with stirring of wind, Neiguan (PC 6) and Taixi (KI 3) were added. Each day, 4 – 5 points of the upper limb and 4 – 5 points of the lower limb were punctured with the uniform reinforcing-reducing method and the needles were retained for 30 min. In addition to the routine drug treatment, based on Xu's MNEFMSA recorded in Zheng Kuishan's *Midnight -Noon Ebb-Flow and the Eight Techniques of Magicturtle* (子午流注与灵龟八法),[6] MNEFMSA group was treated with selecting points and administering acupuncture according to time and date of midnight-noon ebb-flow in rhythm. The selected points were taken as the main points, which were needled first, combined with 1 – 2 adjunct points selected from the upper and lower limbs or the trunk, which were needled later. The needle manipulation and the duration of needle retaining were the same as those of the affected-channel group. The three groups all began their treatments at the period from 7 am to 9 am. Fifteen treatments constituted a course, with 3 – 5 days interval between courses. After two courses of treatment, clinical observations were done on the therapeutic effect, and changes in hemorrheology, IL-6, TXB_2, and 6-keto-$PGF_{1\alpha}$.

Observation indexes and methods

5 ml of fasting venous blood was drawn from each of the patients for hemorheological detection respectively before and after the treatment. The detection indexes included whole blood viscosity (at shear rate of $120s^{-1}$ and shear rate of $10s^{-1}$), plasma viscosity, hematocrit, erythrocyte deformability rate, and erythrocyte aggregation rate. All the detections were done under constant temperature.

For IL-6 determination, all patients had 3 ml venous blood collected in the fasting state respectively before treatment, at the early stage of treatment (one week after treatment) and at the remission stage (30 – 35 days after treatment). The prepared serum samples were kept in the refrigerator at -20℃ to be detected. The reagent kit for IL-6 determination was from Scientific and Technical Development Center of the General Hospital of PLA.

For determinations of TXB_2 and 6-keto-$PGF1_\alpha$, 5 ml of fasting venous blood was drawn from each of the patients through swift venipuncture by a 5 ml disposable syringe with about 0.1 ml of indomethacin and sodium ethylene diamine tetracetate respectively before treatment, at the early stage of treatment and at the remission stage. The blood was homogeneously mixed in the syringe, injected into the test-tube, and then centrifugated at 3500 rpm for 15 minutes at 4℃. The prepared plasma samples were put in the refrigerator at -20℃ to be detected. The radio immunoassay kits for TXB_2 and 6-keto-$PGF1_\alpha$ were respectively from Beijing Yasheng Institute of Biological Technique and Beijing Meidikesheng Biological Technique Ltd.

Statistical methods

Chi-square test was adopted for the intergroup comparison of clinical therapeutic effect. Student's *t* test was adopted for comparison of changes in blood rheology before and after treatment, and changes in IL-6, TXB_2, and 6-keto-$PGF_{1\alpha}$ before treatment, at the early stage of treatment and at the remission stage.

RESULTS

The criteria for clinical therapeutic effect were drawn up based on the *Evaluation Criteria for the Damage of Clinical Nervous Function of Cerebral Apoplexy Patients*. [4] Basically cured: the score of functional damage decreased by 91% – 100%, the degree of disablement was grade 0. Markedly relieved: the score of functional damage decreased by 46% – 90%, the degree of disablement was grade 1 – 3. Improved: the score of functional damage decreased by 18% – 45%. Failed: the score of function damage decreased by 17% or less.

Comparison of the total effective rate among the three groups: Table 1. shows that the total effective rate of MNEFMSA group was significantly superior to that of the drug group ($P<0.01$), and the basic cure rate and the marked relief rate were significantly superior to those of the drug group and affected-channel group ($P<0.05$ or $P<0.01$), suggesting that MNEFMSA can markedly raise the clinical therapeutic effect for acute ischemic cerebrovascular diseases, and the fewer points selected can reduce the patient's sufferings.

Table 1. Comparison of the total effective rate among the three groups (Cases %)

Group	*n*	Basically Cured	Markedly Improved	Improved	Failed	Total
Drug	30	5 (16.67)	3 (10.00)	14 (46.67)	8 (26.67)	22 (73.33)
Channel	30	9 (30.00)	7 (23.33)	11 (36.67)	3 (10.00)	27 (90.00)
MNEFMSA	30	16 (53.33)	9 (30.00)	4 (13.33)	1 (3.33)	29 (96.67)

Comparison of changes in hemorrheology of the three groups: Table 2. shows that before treatment, the hemorrheology of the three groups were abnormal, and after treatment, the various indexes were all markedly improved ($P<0.05$ or $P<0.01$), of which whole-blood viscosity and erythrocyte deformability rate of MNEFMSA group got the most obvious improvement, significantly different from the other two groups ($P<0.05$), suggesting that MNEFMSA group has a better effect than the other two groups in improving hemorrheology, especially in the micro-vessels.

Table 2. Comparison of hemorrheology *before and after treatment among the three groups($\bar{x}$ ±s)*

Group	Time	*n*	Whole bl. vis. (high) (mPa.s)	Whole bl.. vis. (low) (mPa.s)	Plasma vis. (mPa.s)	Hematocrit (%)	EGR (%)	EDR (%)
Drug	Bef. Treat.	30	5.326±0.443	11.764±2.087	1.516±0.175	51.428±5.252	52.553±7.006	49.097±4.854
	Aft. Treat.	30	5.014±0.601*$^{\Delta}$	10.753±1.538*$^{\Delta}$	1.394±0.184*	47.436±4.113**	47.892±5.694**	51.438±4.162*$^{\Delta}$
Channel	Bef. Treat.	30	5.217±0.562	11.984±1.841	1.547±0.158	52.247±5.195	53.143±6.938	49.226±4.657
	Aft. Treat.	30	4.873±0.674*	10.674±1.372**$^{\Delta}$	1.412±0.196**	48.241±4.527**	48.219±5.835**	52.107±4.076*
MNEFMSA	Bef. Treat	30	5.338±0.487	11.856±1.630	1.523±0.182	51.746±5.418	51.887±7.221	49.193±4.268
	Aft. Treat.	30	4.672±0.596**	9.872±1.442**	1.378±0.211**	47.973±4.292**	47.342±5.304**	53.384±3.237**

Note: Intragroup comparison before and after treatment, *P<0.05, **P<0.01; Compared with MNEFMSA group after treatment, $^{\Delta}P$<0.05. EGR denoting erythrocyte aggregation rate and EDR erythrocyte deformability rate.

Comparison of TXB_2, 6-keto-$PGF_{1\alpha}$, and IL-6: Table 3. shows that the three groups all got significant improvement in TXB_2, 6-keto-$PGF_{1\alpha}$, and IL-6 levels at the remission stage as compared with that before treatment (P<0.05 or P<0.01). MNEFMSA group got significant improvement in 6-keto-$PGF_{1\alpha}$ and IL-6 levels ever since the early stage of treatment (P<0.05), suggesting that MNEFMSA can improve the level of IL-6 in the patients, especially at the early stage of treatment, it can help reduce inflammatory and immune reactions and lower the degree of damage to nervous functions so as to promote the recovery of disease, and also decrease effectively TXB_2 but increase 6-keto-$PGF_{1\alpha}$.

Table 3. Comparison of TXB_2, 6-keto-$PGF_{1\alpha}$, IL-6 of patients among the three groups before treatment, at the early stage of treatment and at the remission stage (pg/ml, $\bar{x}$ ±s)

Group	Time	*n*	TXB_2	6-keto-$PGF_{1\alpha}$	IL-6
Drug	Bef. Treat.	30	345.61±261.66	31.45±13.96	207.43±103.93
	Early Stage	30	266.97±179.27	37.81±16.78	168.03±79.78
	Remission	30	204.06±140.80*	74.02±38.32**	111.05±28.24**
Channel	Bef. Treat.	30	337.55±233.23	33.38±19.50	205.29±104.26
	Early Stage	30	274.15±191.49	38.75±13.19	164.19±76.35
	Remission	30	179.85±114.19**	79.46±32.47**	107.84±25.57**
MNEFMSA	Bef. Treat.	30	365.95±286.59	32.55±16.12	208.23±106.08
	Early Stage	30	266.70±177.05	42.16±13.40*	157.83±71.19*
	Remission	30	151.93±88.23**	87.16±32.27**	93.65±16.78**

Note: Intragroup comparison, *P<0.05, **P<0.01.

DISCUSSION

MNEFMSA is an ancient acupuncture method by matching heavenly stems with viscera to treat diseases. The midnight-noon ebb-flow theory holds that when the point is open, *qi* and blood will pour into it, making it hyperactive in action, the acupuncture given at this hour can get twice double the effect. Based on the rhythmic character of the

attacking time of ischemic cerebrovascular diseases, MNEFMSA is adopted for treatment at the corresponding open points during the period from 7 am. to 9 am., which is the opening hour of Stomach Channel of Foot Yangming. *Miraculous Pivot • Meridians* (灵枢经•经脉) states, "Foot Yangming Channel dominates the diseases of blood." Yangming Channel is full of *qi* and blood. Acupuncture treatment given at the open hour can activate the channel-*qi* and dredge the channels and collaterals to replenish *qi* and blood, promote blood circulation by removing blood stasis and regulate *yin* and *yang*, thus the marked therapeutic effect is obtained.

Relevant studies have suggested that the abnormal changes in hemorrheology play a very important part in the whole course of the development of cerebrovascular diseases, [7] and cerebral ischemia is also closely related with inflammatory cell factors. [8] This study also shows that patients with acute ischemic cerebrovascular diseases have abnormal level of IL-6, and those with severer damage of nervous function would have higher level of IL-6 than those with milder damage, suggesting that IL-6 is involved in the occurrence and development of ischemic cerebral diseases and is one of the indexes of damage to the cerebral nervous cells. MNEFMSA can help improve abnormal changes of hemorrheology, lower blood viscosity, decrease thrombosis, raise erythrocyte deformability rate, and as well markedly improve IL-6 level, promote cerebral circulation, increase cerebral volume of blood flow, raise the effective infusion of blood to cerebral tissues, directly improve pathological and physiological changes caused by cerebral ischemia and hypoxia, effectively protect the damaged cerebral tissues, and benefit the recovery of cerebral tissues. The improved level of IL-6 at the early stage of treatment may be significant for improving cerebral damage and decreasing inflammatory and immune reactions. Decreasing the content of TXB_2 and increasing the content of 6-keto-$PGF_{1\alpha}$, especially at the early stage of treatment, to restore the dynamic equilibrium between the two can inhibit gathering of platelet to reduce viscosity of blood, therefore make cerebral vessels expand, lower vascular resistance, improve cerebral blood circulation, increase cerebral blood supply, eliminate cerebral edema, strengthen cerebral infusion, and improve the function of the affected cerebral tissues, hence the marked therapeutic effect is achieved, with a better recovery from AICD.

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